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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	23

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	08/844,215	PERSSON ET AL.	
	Examiner	Art Unit	
	Mary Zeman	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

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A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2001*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-116* is/are pending in the application.

4a) Of the above claim(s) *1-30 and 82-116* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 April 1997* is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☐ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
18)☐ Interview Summary (PTO-413) Paper No(s). _____
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other:

DETAILED ACTION

Continued Prosecution Application

The request filed on 2/16/01 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/844215 is acceptable and a CPA has been established. An action on the CPA follows.

No further amendments or arguments have been filed with the request for the CPA, or as of the date of this action.

Claims 1-116 are pending in this application. Claims 1-30 and 82-116 stand withdrawn from consideration as being drawn to a nonelected invention. These claims should be canceled.

Drawings

The drawings are objected to because Each panel of Figures 1-4 have a blank space where the appropriate SEQ ID NO should be listed. Correction is required.

Proposed drawing corrections must be submitted with the next response. Corrections can no longer be held in abeyance until allowability is noted.

Claim Rejections - 35 USC § 112

Claims 31-33, 48, 56 and 64-81 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth amino acid sequences of various VL and VH regions, some specific nucleotide sequences encoding those sequences and equivalent degenerative codon sequences thereof and therefore the written description is not commensurate in scope with the claims drawn to nucleic acid molecules encoding any naturally occurring VH and VL polypeptides which bind to HCV E2.

Applicant argues in the response of 11/24/99 that the case law cited differs on its face from that of the instant disclosure, and quotes a large portion of the previous written guidelines regarding monoclonal antibodies (proteins). The instant claims are not drawn to antibody *molecules*, (proteins) but to nucleotide sequences *encoding* antibody molecules which are only

defined by their reactivity and specificity. The generic claims of the invention are not supported by the specification as filed, as set forth previously.

It is noted that Applicant's argument at page 4, footnote 2, of the response filed 11/24/99 is factually in error. Applicant argues that the CCPA decision relied upon by the examiner is not controlling as it is not a Federal Circuit decision. This is incorrect and not persuasive. CCPA decisions take precedent over Federal Circuit decisions unless the Federal Circuit decision is *en banc*. See 215 USPQ 657.

The specification discloses SEQ ID NO: 15-27 which corresponds to the genomic DNA encoding the monoclonal antibody variable regions. SEQ ID NO: 15-27 meet the written description and enablement provisions of 35 USC 112, first paragraph. However, claims 31-33, 48, 56 and 64-81 are directed to encompass gene sequences, sequences that hybridize to SEQ ID NO: 15-27, mutated sequences, allelic variants, splice variants, or any nucleotide sequence encoding any antibody variable region which can bind to HCV E2. The claims are not even limited to encoding particular variable regions disclosed by amino acids sequences in the specification. None of these sequences meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 15-27, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable

due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.
>
> The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Therefore, only SEQ ID NO: 15-27, but not the full breadth of the claim, meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-

Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Antibodies to particular antigens are generated by the immune system through random mutation and recombination. (See Kuby, Immunology, Second Edition 1991 WH Freeman and Company, NY Chapter 8 pages 175-204 [previously cited and of record]) The immense variety of the variable regions of antibodies defies prediction of particular nucleic acid sequences. With the exception of the SEQ ID Nos 15-27 setting forth *particular nucleic acid* sequences, the skilled artisan cannot envision the detailed structure of the encompassed polynucleotides which would encode any variable region which would bind to the many epitopes of an HCV E2 protein, and therefore conception is not achieved until reduction to practice has occurred, *regardless of the complexity or simplicity of the method of isolation*. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it.

Support for other nucleic acid sequences encoding VH or VL regions of human antibodies is provided in the specification on page 6, lines 20-25 where it is disclosed that "In another embodiment, the invention is directed to an isolated nucleic acid molecule which contains a polynucleotide coding sequence for a polypeptide that is homologous to the binding portion of a human Fab molecule which exhibits immunological binding affinity for HCV E2 antigen." However, no disclosure, beyond the mere mention of other polynucleotide sequences encoding said Fab fragments is made in the specification. There is no indication how homologous the encoded polypeptides must be to maintain binding affinity for HCV E2, or whether Applicant intends to encompass variable regions of any structure that bind HCV E2. The genus of potential encoding polynucleotides is quite large, and is incredibly diverse such that the specification, as filed, cannot provide adequate written description for it.

Claim Rejections - 35 USC § 103

Claims 31-81 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Mehta et al. (US Patent 5,308,750) in view of Brechot et al (US Patent 5,919,454 with priority under 35 USC 120 to 1993), further in view of Wong et al. for the reasons set forth in the previous office action.

Mehta et al. (US Patent 5,308,750) discloses mouse monoclonal antibodies to the HCV E2 protein. These antibodies or antibody fragments are used in diagnostic assays to detect the E2 antigen in patient samples, and can be labeled with a variety of detection agents (columns 2-4). Mehta et al. state that compositions comprising the monoclonal E2 antibodies are useful for the "diagnosis, evaluation, and prognosis of HCV infection, as well as for studying HCV protein differentiation and specificity." (column 6 lines 23-25) Mehta et al. do not disclose human monoclonal antibodies to the same protein, HCV E2.

Brechot et al (US Patent 5,919,454) discloses human monoclonal antibodies to a related protein, HCV E1 protein (Claims 1-3). Brechot discloses how to prepare, identify and sequence human monoclonal antibodies having the desired specificity, and how to use those human monoclonal antibodies in diagnostic assays for HCV infection (columns 3-4, and Claims 8-10). Brechot et al also disclose F(Ab)2 fragments of those human monoclonal antibodies (column 2 lines 56-67 and claim 4). Brechot does not teach polynucleotides encoding human monoclonal F(Ab)2 fragments to HCV E2.

Wong et al. (Wong et al. 1995 Journal of Investigative Medicine Vol. 43, no.2 Supplement 2 page 397A) discloses a motivation to produce human monoclonal antibodies to HCV E2 so they can be produced recombinantly. Wong discloses that antibodies to E2 could block entry of HCV into the cell, and could potentially be used in a therapeutic composition to inhibit HCV infection.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have produced human monoclonal antibodies to HCV E2, and to have determined the nucleic acid sequences encoding them in view of the disclosures of Mehta et al., Brechot et al. and Wong et al. Recombinant production of monoclonal antibodies is more convenient and less expensive than traditional methods, and human monoclonal antibodies are preferred in passive immunity uses as there are less rejection and undesirable immune responses to the human monoclonal antibodies in comparison to the administration of mouse monoclonals. Brechot discloses that human monoclonal antibodies to HCV proteins are obtainable and desirable, Mehta et al disclose the usefulness of monoclonal antibodies to E2 in diagnostic assays, and Wong et al. provide a motivation to use those human monoclonal antibodies as therapeutic molecules.

Conclusion

No claim is allowed.

This is a CPA of applicant's earlier Application No. 08/844215. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (703) 305-7133. The examiner can be reached between the hours of 7:30 am and 5:00 pm Monday through Thursday, and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at (703) 308-4028.

The fax number for this Art Unit is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst Tina Plunkett whose telephone number is (703) 305-3524.

mkz
May 8, 2001

MARY K ZEMAN
PATENT EXAMINER
AU 1631